Remarks

I. Status of Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-4, 6, 10-12, and 19-36 are pending in the application, with claims 1, 23, 24, and 36 being the independent claims. Claims 5 and 13-18 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 24-36 are sought to be added. Support for the addition of new claims 24-36 may be found in the claims as originally filed, *e.g.*, claims 2-4 and 13-23, and in the specification at, *e.g.*, page 2, line 20 to page 4, line 22, page 9, lines 2-18, and page 10, lines 2-5. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

II. Summary of the Office Action

In the Office Action dated September 24, 2009, the Examiner has objected to claim 15 and has made rejections under 35 U.S.C. § 112, first paragraph, and on the grounds of nonstatutory obviousness-type double patenting. Applicants respectfully offer the following remarks concerning each of these elements of the Office Action.

III. Objection to Claim 15

At page 2 of the Office Action, claim 15 has been objected to for an obvious typographical error, *i.e.*, the claim recites "an polypeptide." Applicants thank the

Examiner for pointing out this error. However, in view of amendments made herein, claim 15 has been cancelled, thus rendering moot the objection. Reconsideration and withdrawal of the objection are respectfully requested.

IV. Rejections Under 35 U.S.C. § 112, First Paragraph, are Traversed

A. Alleged Lack of Enablement of Claims 1-6 and 10-21

At pages 2-5 of the Office Action, claims 1-6 and 10-21 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner has asserted that the specification is allegedly only enabling for "a method of promoting regeneration and survival of dopaminergic neurons in the striatum of mammals injected with 6OHDA (6-hydroxy-dopamine) by administering soluble NgR1 intracranially shortly after injecting 6OHDA," but not for the full scope of the claims. *See* Office Action, pages 2-3. Applicants respectfully disagree.

In order to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, the claimed invention must be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In order to establish a *prima facie* case of lack of enablement, the Examiner has the initial burden to set forth a reasonable basis to question the enablement provided for the claimed invention. *See In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). To satisfy this burden, "it is incumbent upon the Patent Office . . . to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement."

See In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) (emphasis in original).

In addition, Applicants respectfully remind the Examiner that an Applicant is not limited to the confines of the specification to provide the necessary information to enable an invention. *See In re Howarth*, 654 F.2d 103, 105-6, 210 USPQ 689, 692 (CCPA 1981). An Applicant need not supply information that is well known in the art. *See Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997); *Howarth*, 654 F.2d at 105-6, 210 USPQ at 692; *see also In re Brebner*, 455 F.2d 1402, 173 USPQ 169 (CCPA 1972) (finding a disclosure enabling because the procedure for making the starting material, although not disclosed, would have been known to one of ordinary skill in the art as evidenced by a Canadian patent). As discussed below, Applicants submit that it would require no more than routine experimentation for a skilled artisan to practice the full scope of the presently claimed invention in view of the teachings in the specification and the knowledge available in the art. Applicants also submit that the reasons for the rejection, as set forth in the Office Action, are insufficient to establish a *prima facie* case of non-enablement.

The Examiner appears to focus her argument on the alleged breadth of the claims, as embracing "all methods of promoting restoration of dopamine neurons after any injury in the brain involving dopamine neurons, including those involved in human diseases such as Parkinson's disease, and those using any antagonist of NgR besides sNgR1." *See* Office Action, page 3. Applicants respectfully assert that the claims are not overly broad and are fully supported by the specification. However, in an effort to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have

amended claim 1 to recite a method of promoting regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of dopaminergic neuronal degeneration, comprising administering to the mammal a therapeutically effective amount of a soluble form of a mammalian NgR1. In addition, Applicants have added new claim 24, which recites a method of promoting regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of dopaminergic neuronal degeneration, comprising administering to the mammal a therapeutically effective amount of an antibody or antigen-binding fragment thereof that binds to a murine or human NgR1. Furthermore, Applicants have cancelled claims 5 and 13-18, rendering moot the rejection as applied to those claims. Applicants submit that the specification is sufficiently enabling for, and that it would not require undue experimentation to practice, the full scope of the presently claimed invention.

Some experimentation, *e.g.*, testing and screening, even a considerable amount in order to make the invention, is not "undue" if, *e.g.*, it is merely routine. *See In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). As the Examiner points out, Applicants used "conventional tests" in their animal studies of the effects of blocking NgR1 and dopaminergic neuron recovery. *See* Office Action, page 3; specification, pages 16-18. In particular, animal rotational behavior and the dopaminergic neuron-specific injury induced by 6-hydroxydopamine (6-OHDA) used in Applicants animal studies are part of an established model used for screening for anti-Parkinsonian agents as described in Fuxe, K., and Ungerstedt, U., *Pharmac. Ther. B 2*:41-47 (1976) (attached hereto as Exhibit A; "Fuxe"), which is cited at page 16, lines 29-32 of the specification. As described in the specification, Parkinson's disease is associated with progressive

destruction of dopaminergic neurons in the substantia nigra, and 6-OHDA specifically destroys dopaminergic neurons. *See* specification, page 1, lines 10-11 and page 16, lines 21-32; *see also* Fuxe, pages 41 and 46. Thus, using this established model of dopaminergic injury, Applicants found that blocking NgR1, either using a soluble NgR1 polypeptide or a mouse NgR1 knockout strain, increased survival of dopaminergic neurons in the substantia nigra and improved recovery in dopaminergic pathways. *See id.* at pages 16-18. Following the Applicants' Examples, the skilled artisan could readily test and screen additional soluble mammalian NgR1 polypeptides, or antibodies or antigen-binding fragments thereof that bind to a murine or human NgR1, for the ability to promote regeneration or survival of dopaminergic neurons in a mammal.

The Examiner has also asserted that Applicants' claims allegedly "embrace methods of treating all dopaminergic brain disorders, . . . by any means of administration." *See* Office Action, page 4. Applicants respectfully point out that claim 1, and new claim 24, are directed to methods of promoting regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of *dopaminergic neuronal degeneration*, not all dopaminergic brain disorders. Thus, Applicants' claimed methods are applicable to those dopaminergic brain disorders that are characterized by the loss or degeneration of dopaminergic neurons. *See, e.g.*, specification, page 2, lines 6-14. As discussed above, the specification describes an established model of dopaminergic injury using 6-OHDA, which specifically destroys dopaminergic neurons. *See, e.g.*, specification, pages 16-18, Examples 1 and 2; *see also* Fuxe, pages 41 and 46. Thus, this model, which tests whether a particular agent promotes regeneration or increases the survival of dopaminergic neurons, would be applicable to all dopaminergic

brain disorders that are characterized by the loss of dopaminergic neurons. Therefore, following the Applicants' Examples, the skilled artisan could readily apply results from using the model to treat those dopaminergic brain disorders that are characterized by the loss or degeneration of dopaminergic neurons.

Furthermore, Applicants' Examples provide one means of administering the soluble NgR1 polypeptides, *e.g.*, intracranially, in a method of promoting regeneration or survival of dopaminergic neurons. The specification provides additional means well-known to those in the art for administering the specific NgR1 antagonists to a mammal displaying signs or symptoms of dopaminergic neuronal degeneration. *See, e.g., id.* at page 11, line 13 to page 15, line 27. Thus, it would require no more than routine experimentation for a skilled artisan to practice the full scope of the claimed methods in view of the teachings in the specification and the knowledge available in the art.

The Examiner also asserts that the specification allegedly does not enable variants of NgR1, such as recited in claim 6, for use in the methods of the invention. *See* Office Action, page 4. The Examiner further alleges that, in reference to a paper that describes the structural analysis of the soluble ectodomain of NgR1, "the literature is silent as to the differences or changes that are tolerated in NgR's, and by extension sNgR's, while still maintaining the function of binding NOGO ligand (Barton, et al, 2003, 22(13): 3291-3302)." *See id.* at page 5. While the relationship between the sequence of a protein and its biological function may be complex, and it may be difficult to predict the exact functional consequences of a particular mutation, Applicants respectfully point out that in order to use the variants of NgR1 in the claimed methods, a skilled artisan would not need to be able to predict the structural and/or functional

consequences of particular mutations or base changes, *i.e.*, which particular amino acids to change. Rather, the skilled artisan would only need to be able to (a) obtain, *e.g.*, a soluble form of a mammalian NgR1 comprising amino acids 26 to 310 of human NgR1 (SEQ ID NO:3) with up to ten conservative amino acid substitutions, and (b) test them for the ability to promote regeneration or survival or dopaminergic neurons using, *e.g.*, the animal studies described in the specification.

Despite any perceived difficulty in mutating the coding sequence in other receptors as alleged by the Examiner, the skilled artisan could readily ascertain which conservative amino acid substitutions to make in, *e.g.*, SEQ ID NO:3, in view of the specification and the knowledge available in the art. For example, by simply comparing the human and rat NgR1 sequences provided in the specification at page 8, Table 2, the skilled artisan could identify any differences between these conserved sequences which both bind Nogo ligand. In addition, the Barton *et al.* reference identified by the Examiner provides a detailed structural analysis of NgR1 in comparison to other NgR homologs and leucine-rich repeat-containing proteins, to which the skilled artisan could refer for determining what amino acid variations would be tolerated. *See, e.g.*, Barton *et al.*, page 3293, col. 1 to 3298, col. 1 and Figure 2. Once obtained, the soluble NgR1 polypeptides with up to ten conservative amino acid substitutions could be tested in the 6-OHDA animal model provided in the Examples for the ability to increase survival of dopaminergic neurons in the substantia nigra and improve recovery in dopaminergic pathways. Furthermore, using such tests, any inactive variants would be excluded as the method claims are directed to those soluble NgR1 polypeptides that promote

regeneration or survival of dopaminergic neurons, not those variants that do not promote regeneration or survival of dopaminergic neurons.

Accordingly, Applicants submit that a person having ordinary skill in the art, in view of the teachings of the specification and the knowledge in the art, would be able to make and practice the full scope of Applicants' claimed methods. Moreover, Applicants contend that the Examiner has failed to provide acceptable objective evidence or sound scientific reasoning that shows that it would require undue experimentation for a skilled artisan to make and use the claimed invention, and therefore has failed to establish a *prima facie* case of non-enablement. Thus, Applicants respectfully request that this rejection be reconsidered and withdrawn.

B. Alleged Lack of Enablement of Claims 22 and 23

At page 6 of the Office Action, claims 22 and 23 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner has asserted that the specification allegedly "does not reasonably provide enablement for a method of promoting regeneration or survival of dopaminergic neurons in a subject with Parkinson's disease by administering an antagonist of NgR1." *See* Office Action, page 6. Applicants respectfully disagree.

However, in an effort to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 1, from which claim 22 depends, and claim 23 to recite that the methods comprise administering to a mammal a therapeutically effective amount of a soluble form of a mammalian NgR1. In addition, Applicants have added new claims 24, 35, and 36, which recite that the methods

comprise administering to a mammal a therapeutically effective amount of an antibody or antigen-binding fragment thereof that binds to a murine or human NgR1. Applicants submit that the specification is sufficiently enabling for the full scope of claims 22 and 23, as currently presented, and new claims 35 and 36.

As discussed above, Applicants submit that a person having ordinary skill in the art, in view of the teachings of the specification and the knowledge in the art, would be able to make and practice the full scope of Applicants' claimed methods using a soluble form of a mammalian NgR1 or an antibody or antigen-binding fragment thereof that binds to a murine or human NgR1. The Examiner's rejection of claims 22 and 23 appears, however, to focus on a requirement that the Applicants confirm that the claimed methods in fact treat Parkinson's disease. *See* Office Action, page 6 ("The claims embrace a method of treating Parkinson's disease, which is a disease of dopaminergic cell degeneration, without *confirming* that preservation or regeneration of nigral striatal cells in Parkinson's disease involves the NOGO receptor." (emphasis added)). In making these assertions, the Examiner appears to suggest that for the claimed invention to be enabled, Applicants must demonstrate the clinical efficacy of the claimed methods (*i.e.*, that the methods are without obstacles and therapeutically effective) in order to overcome the outstanding enablement rejection. Such a requirement is simply not consonant with the state of the law.

Applicants wish to remind the Examiner that there is no requirement for clinical data to prove that an application is in compliance with 35 U.S.C. § 112, first paragraph. In fact, description of *in vitro* and/or animal testing has been held to enable claims to *in*

vivo therapeutic compositions and methods of their use. To this end, the Federal Circuit has stated that:

> In vitro testing, in general, is relatively less complex, less time consuming, and less expensive than in vivo testing. Moreover, in vitro results with respect to the particular pharmacological activity are generally predictive of in vivo test results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are.

Cross v. Iizuka, 753 F.2d 1040, 1050 (Fed. Cir. 1985); *see also In re Brana*, 51 F.3d 1560, 1567-68 (Fed. Cir. 1995) (holding that animal testing results are sufficient to establish whether one skilled in the art would believe that a pharmaceutical compound has an asserted clinical utility for the purposes of compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph).

The present specification clearly describes methods for use of the soluble NgR1 polypeptides, or antibodies or antigen-binding fragments thereof that bind to a murine or human NgR1, *in vivo* (*see, e.g.*, specification at Examples 1 and 2). Specifically, Examples 1 and 2, describe the increased survival of dopaminergic neurons in the substantia nigra and improved recovery in dopaminergic pathways following injury by reducing NgR1, either with a soluble NgR1 polypeptide or a mouse NgR1 knockout strain. *See* Office Action, pages 16-18. Both of these Examples use 6-OHDA in an established animal model for screening anti-Parkinsonian agents as described in the specification, *see, e.g.*, page 16, lines 23-29, and in Fuxe (Exhibit A), which is cited at page 16, lines 29-32. Under *Cross* and *Brana*, one of ordinary skill would thus recognize that the animal testing described in the present specification would be "generally predictive of *in vivo* test results," *Cross*, 753 F.2d at 1050, and thus would

have a reasonable expectation that the claimed methods would be successful for the claimed *in vivo* therapeutic approaches.

Further, the Examiner's assertion that "recent evidence indicates that cells of the substantia nigra do not express the NgR receptor *at all*," is inaccurate. *See* Office Action, page 6 (emphasis added). A review of the Examiner's evidence in support of this statement, which is Hunt *et al.*, Molecular and Cellular Neuroscience 20:537-552 (2002), indicates that according to Hunt *et al.*, the NgR receptor is expressed weakly or at very low levels in the substantia nigra pars compacta. *See* Hunt *et al.*, page 538, col. 2, pages 540-541, Figure 6, and page 547, col. 1. Weak or very low levels of expression is not the same as no expression at all. In view of the low expression of NgR in the substantia nigra, Hunt *et al.* postulated that "NgR is not a promising candidate for therapeutic intervention in Parkinson's and Alzheimer's diseases," which the Examiner seems to adopt as definitive evidence that Applicants' results described in the Examples would not enable the claimed *in vivo* therapeutic methods. *See id.* at page 543, col. 2; Office Action, page 6. In contrast, however, one of ordinary skill reading Hunt *et al.* and the present specification would recognize the novelty of Applicants' findings and be able to practice the full scope of the claimed *in vivo* therapeutic methods based on the teachings of the present specification.

Therefore, Applicants submit that a person having ordinary skill in the art, in view of the teachings of the specification and the knowledge in the art, would be able to make and practice the full scope of Applicants' claimed invention. As described above, Applicants contend that the Examiner has failed to establish a *prima facie* case of non-enablement. Accordingly, Applicants respectfully request that the rejection of claims 22 and 23 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

C. Alleged Lack of Written Description of Claims 1-6, 10-17, and 19-23

At pages 7-9 of the Office Action, claims 1-6, 10-17, and 19-23 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. In particular, the Examiner has asserted that the Applicants have met the written description requirement for amino acids 26-310 of SEQ ID NO:3 but not for the full breadth of the claims, which are "directed to a method of administering an NgR antagonist to promote survival of dopaminergic neurons in a mammal." *See* Office Action, pages 7 and 9. Applicants respectfully disagree.

However, in an effort to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have amended claim 1 to recite a method of promoting regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of dopaminergic neuronal degeneration, comprising administering to the mammal a therapeutically effective amount of a soluble form of a mammalian NgR1. In addition, Applicants have added new claim 24, which recites a method of promoting regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of dopaminergic neuronal degeneration, comprising administering to the mammal a therapeutically effective amount of an antibody or antigen-binding fragment thereof that binds to a murine or human NgR1. Furthermore, Applicants have cancelled claims 5 and 13-17, rendering moot the rejection as applied to those claims. Applicants submit that the present specification provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the claims, as currently presented.

The Examiner has correctly asserted that "the specification teaches use of the soluble form of NgR," but alleges that the specification only "teaches *an* antibody made

against SEQ ID NO:3." *See id.* at page 7 (emphasis added). Further, the Examiner has asserted that the description of the soluble NgR1 used in the Examples, sNgR(310)Fc, "is not adequate written description of an entire genus of functionally-equivalent polypeptide sequences . . . ." *See id.* at page 8. Applicants respectfully submit that the present claims directed to administering a soluble form of a mammalian NgR1, or an antibody or antigen-binding fragment thereof that binds to a murine or human NgR1, are not overly broad, and that one of ordinary skill could reasonably conclude that the inventors had possession of the presently claimed methods in the specification as filed.

To meet the written description requirement of 35 U.S.C. § 112, first paragraph, an Applicant is not required to disclose or provide a working example of every species of a given genus. *See Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994). According to the Federal Circuit, the disclosure need only recite a representative number of species within the scope of the genus or of structural features common to, and that comprise a substantial portion of, the genus. *See Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568-69, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The Examiner, however, alleges that other than "amino acids 26-310 of SEQ ID NO:3, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides . . . ." *See* Office Action, page 9. Applicants respectfully assert that providing structural features is only one means of providing description, and that Applicants have provided adequate description for the present claims per the Federal Circuit's guidance in *Eli Lilly*.

The present specification describes a number of representative examples of the genus of soluble NgR1 polypeptides and provides detailed specifications for the physical

and/or structural characteristics of other soluble NgR1 polypeptides that would fall within the scope of the present method claims. *See, e.g.*, specification, page 7, line 2 to page 8, line 9. For example, the specification describes four soluble NgR1 polypeptide sequences that can be used in the methods of the invention, not one as asserted by the Examiner, and refers to additional NgR1 polypeptides that were known in the art. *See id.* at page 7, lines 16-21 and page 8, Table 2. The specification also provides structural features that are common to soluble NgR1 polypeptides, and that are required for function, at page 7, lines 13-16 of the specification. In view of these representative species of the genus and the structural features common to the genus of soluble NgR1 polypeptides, a skilled artisan would be able to clearly visualize and recognize the soluble NgR1 polypeptides encompassed by, and used in, the present method claims.

Thus, Applicants respectfully submit that both the "representative number" and the "common structural features" standards under *Eli Lilly* are clearly met by the present specification for soluble mammalian NgR1 polypeptides. In addition, guidance provided by the USPTO's Written Description Training Materials, available at http://www.uspto.gov/web/menu/written.pdf, supports Applicants' contention that the written description requirement is satisfied for the present claims. In particular, the guidance of Example 11B of the Written Description Training Materials supports the written description of Applicants' claim 6 directed to a soluble form of a mammalian NgR1 comprising a peptide, *e.g.*, of amino acids 26 to 310 of human NgR1 (SEQ ID NO:3) with up to ten conservative amino acid substitutions, for use in the methods of the invention.

Example 11B of the Written Description Training Materials involves an analysis of a hypothetical claim involving percent identity: "Claim 2. An isolated nucleic acid that encodes a polypeptide with at least 85% amino acid sequence identity to SEQ ID NO: 2; wherein the polypeptide has activity Y." Written Description Training Materials, Example 11B at page 40. Based on disclosure in the specification of the sequence and domain structure, and an art-recognized structure-function correlation and knowledge of the genetic code, the Written Description Training Materials conclude that the disclosure meets the requirements of 35 U.S.C. § 112, first paragraph. A similar conclusion follows for Applicants' written description of a soluble form of a mammalian NgR1 comprising a peptide, *e.g.*, of amino acids 26 to 310 of human NgR1 (SEQ ID NO:3) with up to ten conservative amino acid substitutions, for use in the methods of the invention

For example, as in Example 11B of the Written Description Training Materials, "[t]he disclosure of [SEQ ID NO:3] combined with the knowledge in the art regarding the genetic code would have put one in possession of the genus of" polypeptides. *Id.* at 41. With the aid of a computer, one of ordinary skill could list all of the polypeptides with up to ten conservative amino acid substitutions in amino acids 26 to 310 of SEQ ID NO:3.[1] *Id.* Further, the instant specification identifies domains responsible for activity in which the ordinarily skilled artisan "would expect that many of the conservative substitutions would result in a protein" for use in the methods of the invention, *i.e.*, that promotes regeneration or survival of dopaminergic neurons. *See, e.g.*, specification, page 7, lines 13-21, and pages 16-18, Examples 1 and 2; *see* Written Description

[1] Applicants note that a peptide with up to ten conservative amino acid substitutions of amino acids 26 to 310 of SEQ ID NO:3 would have a percent identity of approximately 96% or greater when compared to amino acids 26 to 310 of SEQ ID NO:3 without substitutions, which is much higher than the percent identity of 85% recited in Example 11B.

Training Materials, pages 41-42. Moreover, in view of the disclosure and the knowledge in the art regarding NgR1 structure and function, *see, e.g.*, specification, page 7, lines 20-21 (International Patent Appl. Nos. PCT/US02/32007 and PCT/US03/25004) or Barton *et al.*, page 3293, col. 1 to 3298, col. 1 and Figure 2, "a correlation exists between the function of the claimed protein and the structure of the disclosed . . . [soluble NgR1] domains." Written Description Training Materials, page 42. Therefore, based on Applicants' "disclosure and the knowledge within the art, those of ordinary skill in the art would conclude that the [Applicants] would have been in possession of the claimed genus of " soluble mammalian NgR1 polypeptides comprising a peptide, *e.g.*, of amino acids 26 to 310 of human NgR1 (SEQ ID NO:3) with up to ten conservative amino acid substitutions, for use in the methods of the invention. *Id.*

Applicants also respectfully submit that both the "representative number" and the "common structural features" standards under *Eli Lilly* are clearly met by the present specification for antibodies or antigen-binding fragments thereof that bind to a murine or human NgR1. For example, the specification describes a representative number of antibodies or antigen-binding fragments thereof that bind to a murine or human NgR1. *See, e.g.*, specification, page 3, line 21 to page 4, line 5. The specification also provides structural features that are common to the antibodies or antigen-binding fragments thereof, and that are required for function. For example, at page 9, lines 2-5 of the specification, the antibodies or antigen binding fragments thereof "specifically bind[] an immunogenic Nogo receptor-1 polypeptide and inhibit[] the binding of Nogo receptor-1 to a ligand (*e.g.*, NogoA, NogoB, NogoC, MAG, OM-gp)." Further, the specification provides a description of NgR1 antigens from human and rat NgR1, and a correlation

between structure and function of the disclosed NgR1 proteins that would allow the ordinarily skilled artisan to recognize other NgR1 proteins, and antibodies that bind thereto, encompassed by the presently claimed genus. *See, e.g., id.* at page 3, line 26 to page 4, line 5, page 7, lines 13-21, page 8, Table 2. In addition, as noted in the specification, methods of making antibodies were well known in the art. *See, e.g., id.* at page 10, line 2 to page 11, line 2. Thus, one of ordinary skill in the art would have recognized that the disclosure of the human and rat NgR1 polypeptides put Applicants in possession of antibodies or antigen binding fragments thereof that bind to a murine or human NgR1.

In view of these arguments, Applicants respectfully assert that sufficient description is provided for the present method claims directed to the use of those antibodies or antigen-binding fragments that bind to a murine or human NgR1 and promote regeneration or survival of dopaminergic neurons in a mammal displaying signs or symptoms of dopaminergic neuronal degeneration. Therefore, based on Federal Circuit precedent and the guidance provided by the USPTO, Applicants submit that there is adequate written description for claims 1-4, 6, 10-12, 19-23, and 24-36. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

V. Double Patenting Rejection is Traversed

At page 9 of the Office Action, claims 22 and 23 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 103 and 104 of U.S. Patent Appl. No. 12/335,328. Applicants respectfully traverse this rejection. However, Applicants respectfully request that this rejection be held in abeyance until subject matter that is otherwise patentable is identified.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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